Sleep and Depression in Combat-Related PTSD Inpatients

Steven H. Woodward, Matthew J. Friedman, and Donald L. Bliwise

The sleep of 27 unmedicated Vietnam combat–related posttraumatic stress disorder (PTSD) inpatients was monitored for 3 nights. Depressive comorbidity was considered both as a diagnostic category using DMS-III-R criteria, and as a continuous variable using the Beck Depression Inventory (BDI). Data collected included sleep architecture features that have discriminated unipolar depressives from controls in many prior studies, rapid eye movement (REM) sleep latency, and slow-wave sleep time, as well as two additional indices that have sometimes discriminated depressives from controls in waking studies—baseline heart rate and facial electromyography. Structured Clinical Interview for the DSM-111-R (SCID)-diagnosed PTSD + major depressive disorder (MDD) patients failed to exhibit shorter REM latencies, greater REM percents of sleep, or greater REM densities than PTSD − MDD patients, but did exhibit less slow wave sleep. PTSD + MDD patients also exhibited less facial (mentalis) electromyographic activity. REM densities and baseline heart rates were equivocal. REM density, baseline heart rate, and mentalis electromyography all correlated with the BDI, the former two positively, the last, negatively. In summary, SCID-diagnosed PTSD + MDD patients failed to exhibit the classic REM sleep architectural modifications associated with unipolar depression, despite the fact that several other psychophysiologic indices of dysphoria were detectable in their sleep.

Key Words: Sleep, stress, trauma, depression, EMG

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Introduction

Many patients with chronic severe posttraumatic stress disorder (PTSD) concurrently meet criteria for major depressive disorder (MDD). Lifetime prevalence rates of MDD in outpatients with active PTSD have ranged as high as 65% (Escobar et al 1983; McFarland 1985; Kulka et al 1988). These high rates of depressive comorbidity, as well as the widespread use of antidepressants in pharmacotherapy for PTSD, add weight to the questions raised by apparent biological differences between these disorders. Whereas MDD is associated with hypercortisolemia (Carrol et al 1976a), PTSD is associated with reduced urinary free-cortisol (Mason et al 1986; Yehuda et al 1990) and with increased numbers of glucocorticoid receptors (Yehuda et al 1991). Whereas depression is associated with

From the National Center for Post-Traumatic Stress Disorder, Clinical Laboratory and Education Division, DVAMC, Palo Alto, CA (SHW); the National Center for Post-Traumatic Stress Disorder, Executive Division, DVAMC & ROC, White River Junction, VT, and the Departments of Psychiatry and Psychopharmacology, Dartmouth Medical School, Dartmouth, NH (MJF); and the Sleep Disorders Center, Department of Neurology, Emory University School of Medicine, Atlanta, GA (DLB).

Address reprint requests to Steven H. Woodward, Ph.D., NCPTSD Sleep Lab, VAMC 323-D6, 3801 Miranda Ave., Palo Alto, CA 94303.

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relative insensitivity to the dexamethasone suppression test (DST; Carrol et al 1976b; Carrol 1984), this appears reversed in PTSD. Halbreich et al (1990) failed to find nonsuppression to a large dose of dexamethasone a sample of 14 combat-related PTSD cases who concurrently met criteria for endogenous MDD. Yehuda et al (1993a) observed cortisol suppression in half the typical dose of dexamethasone in a combat-related PTSD sample. These data suggest that the negative feedback mechanism responding to dexamethasone challenge is enhanced in PTSD, possibly due to lower-than-normal basal cortisol levels in this population (see Yehuda et al 1993b for a review of this area of research).

Because of its potential relevance to treatment, untangling depression and PTSD would seem to be a valuable goal for research in this arena. An important class of biological markers that can be brought to bear on this question are sleep variables. Fifty to 70% of adult unipolar depressives exhibit mean rapid eye movement (REM) sleep latencies (the length of time between sleep onset to the beginning of the first REM period), which are 30–40% shorter than controls (for reviews see Kupfer and Foster 1978; Reynolds and Kupfer 1987, 1988), though the specificity of this and related REM findings to depression has been challenged (Zarcone et al 1987; Benca et al 1992). In PTSD samples presumably heterogeneous for comorbid depression, REM latency has been reported to be shortened (Greenberg et al 1972; Kauffman et al 1987) and lengthened (Schlosberg and Benjamin 1978; Lavie et al 1979; Hefez et al 1987; Glaubman et al 1990). Similarly, REM time (or percent of sleep) has been reported to be both increased (van Kammen et al 1990) and decreased (Schlosberg and Benjamin 1978). Differences in the distributions of depressive comorbidity in these samples may account for this divergence of findings. The present study was designed to address this question by measuring REM latency, REM percent, and REM density in closely matched groups of combat-related PTSD patients differing in Structured Clinical Interview for DSM-III-R (SCID)-diagnosed depressive comorbidity.

Although there exists a long line of studies of REM architecture in depression, other psychophysiological markers that have distinguished depressives from controls in waking studies may be examined in sleep. Waking baseline heart rate (HR) differences between depressed patients and controls have been observed by a number of investigators (McCarron 1973; Dawson et al 1977 1985; Lake et al 1982; Iacono et al 1983; Carney et al 1988), one study reporting a diagnostic sensitivity of 85% and specificity of 95% for elevated resting heart rate in unipolar depression (Dawson et al 1985). Among the studies that have examined sleep HR in depression, baseline elevation has been observed in some (Lahmeyer and Beller 1987; Goetze and Tolle 1988), but not others (Keshevan et al 1987). Most of these studies, however, like most studies of waking baseline HR, have relied on repeated point measurements of 1–3-minute epochs, such that the sum total of minutes of electrocardiogram (ECG) rate-analyzed has represented only a tiny fraction of the collected data. The present study will reexamine this issue utilizing computer-assisted quantification of two full postadaptational nights of digitized ECG.

Studies of facial electromyography (EMG) in normal subjects during experimental mood inductions have reliably observed enhancements of corrugator ("frown muscle") EMG during negatively valenced imagery and enhancements of zygomatic ("smile muscle") EMG during positively valenced imagery (see Dimberg 1990 for a review). Depressed patients reliably exhibit attenuation of the positive-valence pattern when attempting to generate positive imagery (Schwartz et al 1976a, b; Greden et al 1986). Conversely, elevated baseline EMG tone across corrugator and zygomatic muscles has predicted positive treatment response in clinically depressed samples (Schwartz et al 1978; Carney et al 1981; Greden et al 1984). In this study, we digitized and quantified EMG activity at the mentalis (chin) and anterior tibialis (leg) sites traditionally recorded in polysomnography. The findings of Schwartz et al (1976a) suggest that mentalis EMG generally follows zygomatic and demonstrates an accentuated response to positive imagery in normals. We were therefore interested in whether spontaneous mentalis EMG bursting during sleep would be attenuated in depressed PTSD patients. The algorithm used quantified the durations of brief EMG increases, or bursts, over and above local baseline.

Methods

All subjects were inpatients on the Specialized Inpatient PTSD Unit at the DVAMC, Palo Alto, California (Menlo Park Division). The Structured Clinical Interview for the DSM-III-R (SCID) (Spitzer et al 1990) and the Clinician Administered PTSD Scale (CAPS) (Blake et al 1991) were administered to all patients to obtain a SCID-based diagnosis for Axis I psychopathology other than PTSD and a CAPS-based diagnosis for PTSD. A battery of self-report instruments was administered to all patients, including the Combat Exposure Scale (CES) (Keane et al 1989), the Mississippi Scale for Combat-Related PTSD (MISS) (Keane et al 1988), the MMPI-2 (Butcher et al 1989) from which was extracted the PK scale (a criterion-keyed scale for PTSD; Keane et al 1984), the Beck Depression Inventory (BDI) long form (Beck et al 1961), and the Beck Anxiety Scale (BANX) (Beck et al 1988). Self-report

instruments were administered at admission and interviews were performed 2–4 weeks later.

Potential subjects were screened for medical diseases and/or chronic pain which could influence sleep, and for obvious indications of obstructive sleep apnea (frequent snoring, obesity, reports of breath stoppage during sleep, prior sleep study indicating sleep apnea). Because recent alcohol intake can markedly affect sleep architecture, potential subjects were excluded if they reported a period of alcohol intake greater than 5 ounces per day for 30 consecutive days during the 6 months prior to the study. Because subjects were typically tested 1–2 months post-admission (mean = 37 days), the majority had been substance-free for at least 60 days prior to laboratory sleep assessment. For three subjects who had been recently withdrawn from psychotropic medications, washout periods exceeded 10 half-lives (nortriptyline, 14 days; imipramine, 10 days; trazodone, 8 days). Data from tested subjects were excluded from statistical analysis if there was objective evidence of sleep apnea with severity greater than 10 apneas/hypopneas per hour on any lab night. Subjects were also excluded if there was objective evidence of periodic leg movements of sleep resulting in repeated arousals (Coleman 1982). The final sample included 27 subjects. All were males ranging from 39–48 years in age (mean 45, SD 2.8). All met criteria for current PTSD on the CAPS. Seventeen met criteria for current MDD on the SCID (PTSD + MDD); 10 did not meet MDD criteria (PTSD − MDD). Among the PTSD − MDD subjects, 5 met criteria for past MDD, while 5 did not. The PTSD + MDD and PTSD − MDD subsamples did not differ in the rates of SCID diagnosis for alcohol/substance dependence. The sample included 20 subjects (74%) with a history of alcohol abuse/dependence and 21 (78%) with a history of nonalcohol substance abuse/dependence. Fifteen subjects (56%) were positive for both alcohol and substance abuse, and 4 subjects (15%) had negative abuse histories. The PTSD + MDD and PTSD − MDD subsamples did not differ in the rates of SCID diagnosis for non-PTSD anxiety disorders, such as panic disorder, agoraphobia without history of panic, generalized anxiety disorder, social phobia, obsessive-compulsive disorder, or simple phobia.

Subjects giving informed consent were asked to arrive at the sleep lab 1.5 hours prior to their desired bedtimes. The laboratory is contained in the inpatient unit and the beds and bedding used were those to which subjects were accustomed. Subjects brought whatever personal effects were part of their normal bedtime customs. They were informed that they could signal the technician at any time for assistance in getting up during the night. Subjects terminated their sleep at will or, if still sleeping, were aroused at 6:00 AM, the standard time for the inpatient treatment program. The recording montage included two channels of bipolar electrooculogram (EOG) and four channels of scalp electroencephalogram (EEG) at F3, F4, Cz, and Pz sites referred to linked mastoids. EOG and EEG were filtered to a 0.3 to 30 Hz bandwidth. Surface EMG was recorded from mentalis and left anterior tibialis. EMG was filtered to a bandwidth of 10–100 Hz. EMG was rectified and integrated over a 20-msec time constant (Coulbourn S76-01 contour-following integrators) prior to digitization. Also recorded were ECG (lead 2; filtered to 1–30 Hz), respiratory effort (via Grass Instruments respiratory transducer) and blood oxygen saturation (Ohmeda 3700 oxymeter). All data were digitized at 125 Hz and streamed to disk using a CODAS wave-scroller/data-acquisition interface (DATAQ Instruments, Akron, OH) hosted in a PC laboratory computer.

Manual scoring of paper records was performed by trained sleep technicians following the Rechtschaffen and Kales (1968) criteria applied to 30-sec epochs. Indices of sleep architecture extracted from manual scoring of sleep records included time in bed, time asleep, times in stages 1, 2, 3, 4, and REM, awake and movement times, and latencies to stages 1 and 2 sleep (without correction for intercurrent awake). REM latencies were scored from both stage 1 onset and stage 2 onset without correction for intercurrent awake time. Computer-based algorithms written by the first author were used to calculate REM densities, HRs, and EMG burst rates per epoch of sleep. The eye movement detection algorithm first filtered the raw EOG to a 0.1–7 Hz bandwidth, then quantified the number of 0.5-sec subepochs of EOG activity whose sample variances exceeded the lowest octile of the set of all 60 0.5-sec subepoch variances in the current 30-sec sleep epoch. Thus, the algorithm detected second-order deviations from the statistics of the signal epoch, capitalizing upon the fact that exclusive of actual eye movements, EOG during REM sleep is typically quiescent. This approach also allowed for straightforward quantification of eye movement amplitude per unit time, though such data proved to correlate highly with numbers of EOG activity units and will not be reported here. HR was estimated via detection of R-waves in the digitized ECG. Artifact detection methods were applied both during signal analysis and during later review of per-epoch values. EMG bursting was scored whenever the EMG level exceeded three standard deviations above the mean of the quietest 1-sec subepoch of the current 30-sec epoch of sleep. Threshold values were recalculated per 30-sec epoch, factoring out variations in baseline muscle tone. For all per-epoch scored indices (REMs, HR, and EMG bursting), per-night values were derived by calculating the medians of all values associated with specific sleep stages: awake, 1, 2, 3, 4, and REM. The computer scoring of REMs, HRs,

BIOL PSYCHIATRY
1996;39:182–192

Table 1. Sleep Architecture by Group

	PTSD − MDD	PTSD + MDD	Significance
Time in bed[a]	394 (53)	401 (52)	NS
Asleep	368 (46)	375 (55)	NS
Awake	29 (23)	29 (24)	NS
Stage 1	47 (17)	52 (23)	NS
Stage 2	196 (54)	216 (34)	NS
SWS	31 (29)	11 (13)	$p = 0.02$
REM	94 (12)	97 (31)	NS
Latency to stage 1	4 (2)	8 (8)	NS
Latency to stage 2	11 (6)	17 (14)	NS
REM lat fr stage 1	70 (14)	66 (40)	NS
REM lat fr stage 2	65 (12)	67 (27)	NS
Sleep efficiency	93 (4)	92 (6)	NS
Stage 1 %	11 (3)	13 (5)	NS
Stage 2 %	48 (10)	53 (7)	NS
SWS %	9 (9)	3 (3)	$p = 0.02$
REM %	24 (3)	23 (6)	NS

[a]All values are in minutes. Standard deviations are in parentheses.
[b]In all cases, t is evaluated over df = 25.

and EMG by reference to sleep stage was enabled by a system that registered digital data and paper scoring with an accuracy of +/−1 second all night. This paper-referenced system also allowed for manual exclusion of artifactual and out-of-bed epochs. The per-subject values presented below are, in all cases, means calculated over nights 2 and 3. The C language code for all signal processing tasks we performed will be provided upon request.

Results

The PTSD − MDD group tended to report reduced symptomology across psychometric instruments. This trend reached significance for Minnesota Multiphasic Personality Inventory-2 (MMPI-2) scales F (69 vs. 92, $t(23) = -2.789$, $p = 0.01$) and 8 (72 vs. 88, $t(23) = -2.403$, $p = 0.025$; MMPI-2 data were missing for two subjects), but was apparent also on the MISS (112 vs. 120), BDI (21 vs. 24), BANX (21 vs. 27), and MMPI-2/PK scale (30 vs. 33). In contrast, PTSD − MDD subjects actually reported significantly higher mean CES scores than the PTSD + MDD subjects (28 vs. 22, respectively, $t(25) = 2.382$, $p = 0.025$). A comparison of remitted and never-depressed PTSD-MDD subjects found no significant psychometric differences or trends.

Sleep architecture differences between the groups were small (see Table 1). In particular, there were no REM architecture trends in the expected direction of earlier and more abundant REM sleep in the PTSD + MDD group. Figure 1 depicts the distributions of REM latencies from stage 1 for the PTSD − MDD and PTSD + MDD groups. It is apparent from this plot that the PTSD + MDD group included two subjects exhibiting so-called sleep-onset REM periods (SOREMPs). Analyzing REM latencies from stage 2 factored out the effect of SOREMPs. Whether computed from stage 1 or stage 2, however, REM latencies within the normal range of 65–70 minutes for both groups. REM latency variance differences between groups were significant when REM latency was calculated from stage 1 and including the SOREMPs ($F(16,9) = 4.45$, $p < 0.015$). It was nearly significant when calculated from stage 2 ($F(16,9) = 2.94$, $p < 0.06$) excluding the SOREMPs. There was no segregation of REM latencies within the PTSD − MDD group according to whether or not subjects met criteria for past MDD. Significant PTSD + MDD/PTSD − MDD group differences were apparent in slow-wave sleep (SWD; stages 3 + 4), which was more abundant in the PTSD − MDD group. Never-depressed members of the PTSD − MDD group appeared to account for most of this difference, exhibiting significantly more SWS than remitted members of that group (14.3% vs. 3.3%, respectively; $F(1,8) = 5.8$, $p < 0.05$). Parenthetically, when we tested the impacts of alcohol and substance abuse history on SWS, by performing ANOVAs in which these factors were crossed with cormorbid MDD, no effects or interactions were association with abuse history (all Fs < 1.0). In each case, the effect of MDD was preserved. As the effects of recent alcohol abuse on SWS are particularly well established (c.f. Benca et al 1992), this null result suggests that substance abuse history did not substantially affect or confound analyses of other sleep variables in this study, despite the high rate of abuse history.

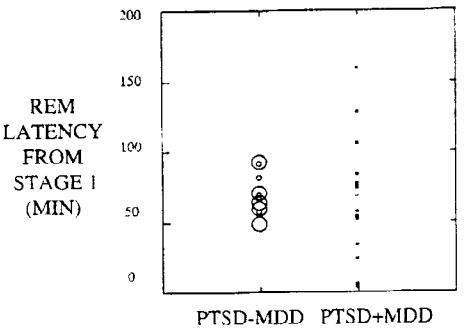

Figure 1. Distributions of REM latencies from stage 1 for the PTSD − MDD and PTSD + MDD groups. In this and all subsequent plots, PTSD + MDD subjects are plotted with small squares, PTSD − MDD subjects meeting criteria for past MDD, now in remission, with small circles, and never-depressed PTSD − MDD subjects with large circles.

Table 2. REM Density (Number of Criterial Subepochs) by Group, Direction, and Metric

Criterial subepochs[a]	PTSD − MDD	PTSD + MDD	
Vertical	4.9 (1.4)	6.3 (1.6)	$p = 0.039$
Horizontal	6.7 (1.5)	6.3 (2.5)	NS
Oblique	7.2 (2.2)	8.4 (2.6)	NS

[a]Standard deviations are in parentheses.

Table 2 presents REM density means and standard deviations for the PTSD − MDD and PTSD + MDD groups. Weak trends were observed wherein PTSD + MDD subjects exhibited slightly higher REM densities. These reached nominal significance for numbers of criterial epochs of vertical EOG. Figure 2 depicts the distributions of numbers of criterial 0.5-sec epochs of vertical REM activity by group. SOREMP subjects exhibited REM EOG activities near the mean of the PTSD + MDD sample and therefore exerted no undue leverage in these analyses.

As noted in the introduction, a number of earlier studies of biological markers of depression in PTSD have failed to find predicted differences across SCID-diagnosed PTSD + MDD and PTSD − MDD groups. An explanation applicable both to earlier findings and to those of the current study is that the diagnosis of comorbid MDD in the context of PTSD is difficult to make, due to symptom overlap. Discordant reports of depressive symptomology on interview and on the BDI may be viewed as evidence of compromised diagnostic accuracy. Such discordant reports were evident in these data as indicated in Figure 3. Additional explanations may be advanced for these discordances, including the fact that the assessments were made weeks apart and under different conditions. In order to reduce the likelihood of classification inaccuracy from all sources, we formed two new groups using both SCID diagnoses and BDI scores: a −/−MDD group ($n = 7$) was

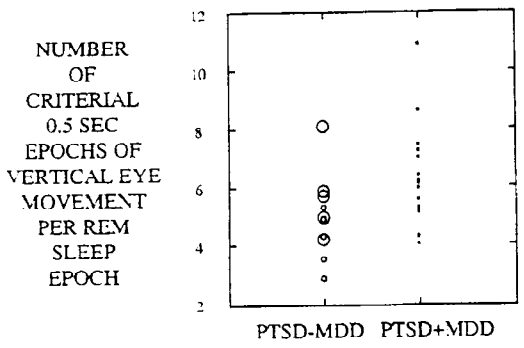

Figure 2. Distributions of numbers of the criterial 0.5-second epochs of vertical REM activity per 30 seconds of REM sleep for the PTSD − MDD and PTSD + MDD groups.

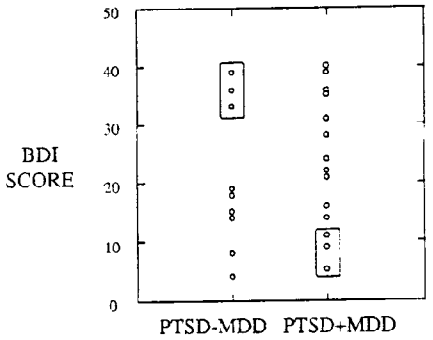

Figure 3. Distributions of BDI scores for the PTSD − MDD and PTSD + MDD groups. Boxes indicate markedly discordant cases.

SCID-diagnosed free of current MDD and exhibited a BDI score below a median split of all scores (mean = 14), while a +/+MDD group ($n = 10$) was SCID-diagnosed with current MDD and exhibited a BDI score above a median split of all scores (mean = 32). These two groups also did not differ in REM latency (from stage 1: 71 vs. 72 minutes, respectively; from stage 2: 68 vs. 69 minutes), in REM time (95 vs. 86 minutes, respectively), or in REM% (24 vs. 21%).

Table 3 presents HR means and standard deviations for the SCID-diagnosed PTSD − MDD and PTSD + MDD groups. Due to ECG artifact and the small amount of SWS in this sample, 10 cases were missing HR estimates from SWS. Accordingly, only stage 2 and stage REM HRs, for which estimates could be derived from all subjects, were analyzed. The within-subjects effect of stage, in which HRs were approximately 1 beat/min (BPM) higher in REM, was significant ($F(1,25) = 5.5$, $p = 0.027$). There was no SCID-diagnosed group effect on HR (63.7 vs. 64.1 BPM for the PTSD − MDD and PTSD + MDD groups, respectively) nor an interaction between group and stage; however, when the conjointly diagnosed −/−MDD and +/+MDD groups were compared, differences in HR approached significance (61.3 vs. 65.8 BPM, respectively; $p < 0.07$).

Table 4 presents mean mentalis EMG burst rates and standard deviations by site for the SCID-diagnosed PTSD

Table 3. Heart Rate (HR) by Group and Stage[a]

	PTSD − MDD	PTSD + MDD	Significance
HR, stage 2	63.3 (7.2) [10]	63.4 (6.5) [17]	NS
HR, REM	64.0 (8.4) [10]	64.6 (5.0) [17]	NS

[a]Standard deviations are in parentheses. Sample Ns are in brackets. Sample Ns were reduced in some comparisons because only a subset of subjects provided enough artifact-free ECG epochs in association with a particular sleep stage to estimate a mean HR for that stage. Many subjects exhibited little or now slow-wave sleep, leading to sample reductions for those comparisons.

Table 4. Electromyelography (EMG) Burst Rates by Group and Stage

Mentalis burst rate[a]	PTSD − MDD	PTSD + MDD	Significance
Stage 1	3.3 (1.7) [10]	2.2 (0.86) [17]	$p = 0.036$
Stage 2	1.15 (0.93) [10]	0.55 (0.29) [17]	$p = 0.020$
REM	1.4 (0.63) [10]	0.77 (0.34) [17]	$p = 0.003$

[a]Values are seconds of EMG bursting per 30-second epoch of sleep. Standard deviations are in parentheses. Sample Ns are in brackets. Sample Ns were reduced in some comparisons because only a subset of subjects provided enough artifact-free EMG epochs in association with a particular sleep stage to estimate a mean EMG burst rate for that stage. Many subjects exhibited little or no slow-wave sleep, leading to the sample reductions for those comparisons.

− MDD and PTSD + MDD groups. What follows is limited to the analysis of median mentalis EMG bursting durations for stages 1, 2, and REM, which could be estimated in all subjects. A significant main effect of group was observed, with PTSD + MDD subjects demonstrating lower EMG burst rates overall ($F(1,25) = 7.1$, $p < 0.01$). A main effect of stage was also obtained (stage 1 > stage REM > stage 2; $F(2,50) = 93.0$, $p < 0.001$). Figure 4 plots the distributions of REM mentalis EMG bursting (sec/epoch) over PTSD − MDD and PTSD + MDD groups. In this figure, strong segregation is apparent

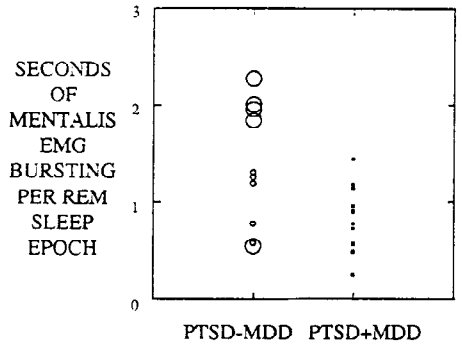

Figure 4. Distributions of seconds of mentalis EMG bursting per 30-second epoch of REM sleep for the PTSD − MDD and PTSD + MDD groups.

with the PTSD − MDD group. Four of five never-depressed subjects exhibited substantially more mentalis EMG bursting than PTSD − MDD patients with a positive history of MDD, whereas the latter demonstrated EMG bursting similar to that of currently depressed PTSD + MDD patients. Within the PTSD − MDD group, itself, differences in EMG bursting between never-depressed and remitted subjects were statistically significant ($F(1,8) = 8.4$, $p = 0.02$).

In addition to group effects, we were interested in correlations between sleep variables and depression evaluated as a continuous variable. Table 5 presents a matrix of rank-order correlations among a reduced set of the variables assessed. Observable within this matrix were significant positive correlations between HR and both BDI and MISS, and significant negative correlations between stage REM mentalis EMG and BDI and between stages 2 and REM mentalis EMG and MISS. HR and EMG indices were not, themselves, correlated. This is understandable, in light of the fact that the amounts of EMG bursting observed outside of stage 1 were less than 1 sec per 30-sec epoch of sleep, and were therefore probably insufficient to recruit additional cardiac output. Given the low correlation between HR and mentalis EMG, it was of interest to determine, through multiple regression, whether they could cojointly provide an improved prediction of BDI scores. Calculated over all 27 subjects, mentalis EMG bursting and baseline HR from stage REM each captured significant unique variance in BDI scores leading to an adjusted multiple R^2 of 0.37 ($F(2,24) = 8.7$, $p < 0.001$). BDI and MISS were highly correlated as well, and a very similar multiple regression result was obtained when MISS was substituted for BDI in the above model (adjusted multiple $R^2 = 0.32$ ($F(2,24) = 7.2$, $p < 0.004$). The addition of REM density did not improve the prediction of BDI or EMG is the whole data set. Figure 5 presents scatterplots involving BDI, MISS, HR, and EMG. Notable in the scatterplots involving EMG was a tendency

Table 5. Rank-Order Correlations among Psychometric and Psychophysiologic Indices

	BDI	MISS	REM LAT	REM %	REM EOG	SWS %	HR REM	HR 2	ME EMG 2
MISS	0.729***								
REM LAT	−0.069	−0.069							
REM %	−0.258	−0.167	−0.505**						
REM EOG	0.399*	0.265	0.032	−0.271					
SWS %	0.221	0.122	0.074	0.119	−0.048				
HR REM	0.600***	0.489**	−0.047	0.013	0.199	0.317			
HR 2	0.510**	0.377	−0.045	0.032	0.056	0.301	0.933***		
ME EMG 2	−0.232	−0.486**	0.261	0.006	0.012	0.314	−0.080	−0.090	
ME EMG REM	−0.455*	−0.505**	0.087	−0.043	−0.106	0.075	−0.303	−0.239	0.674***

BMI = Beck Depression Inventory; MISS = Mississippi Scale for Combat-Related PST; REM = rapid eye movement; LAT = latency; EOG = electrooculogram; SWS = slow-wave sleep; HR = heart rate; ME = TK; EMG = electromyelography.

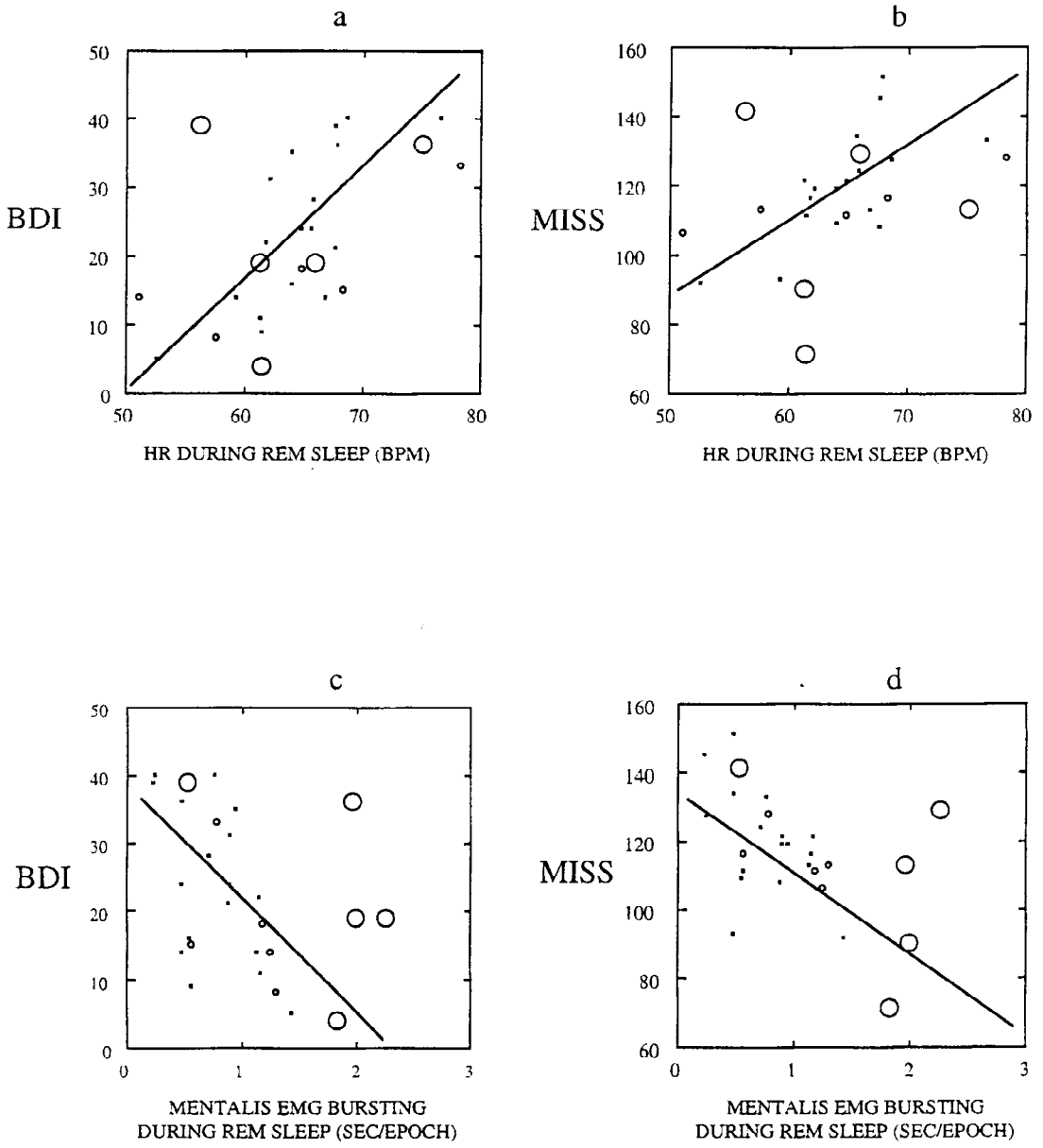

Figure 5a–d. Scatterplots of (a) REM sleep baseline HR × BDI, (b) REM sleep baseline HR × MISS, (c) REM sleep mentalis EMG bursting × BDI, and (d) REM sleep mentalis EMG bursting × MISS. Least-squares regression lines are plotted for the PTSD + MDD groups, only. HR = heart rate; MISS = Mississippi Scale for Combat-Related PTSD; BDI = Beck Depression Inventory; EMG = electromyography.

for members of the never-depressed subgroup of PTSD − MDD patients to lie outside of the main bivariate distributions. In contrast, the remitted members of the PTSD − MDD group were distributed among the currently depressed subjects. When the never-depressed subjects were excluded, correlations between BDI, MISS, HR, and EMG were predictably higher (BDI × HR: $r = 0.718$, $p < 0.001$; BDI × REM mentalis EMG: $r = -0.533$, $p < 0.011$; MISS × HR: $r = 0.642$, $p < 0.002$; MISS × REM mentalis EMG: $r = -0.485$, $p < 0.021$). Conjoint predictions using stage REM HR and mentalis EMG bursting were similarly improved (BDI: adjusted multiple $R^2 = 0.47$; MISS: adjusted multiple $R^2 = 0.38$). Finally, with never-depressed subjects removed, the addition of REM density (numbers of oblique movements) markedly improved the prediction of BDI but not MISS

scores (BDI: adjusted multiple $R^2 = 0.63$; MISS: adjusted multiple $R^2 = 0.37$).

Discussion

PTSD + MDD patients did not exhibit the expected reduction of REM latency and increase in REM sleep percent typically seen when unipolar depressed patients are compared with nondepressed controls. Mean REM latencies from stage 1 sleep, 70 minutes for the PTSD − MDD group and 66 minutes for the PTSD + MDD group, were both close to the value of 72 minutes reported as normative REM latency for men aged 40–49 by Williams et al (1974). When REM latency from stage 2 sleep was examined, the group means were only 2 minutes apart (65 vs. 67 minutes). These results did not change when subjects were conjointly classified using both the SCID and BDI. PTSD + MDD and PTSD − MDD groups came close to differing in the variability of REM latency, which was marked in the former (PTSD + MDD group range 22–127 minutes, SOREMPs excluded, mean of two post-adaptational nights).

Despite the absence of group differences in REM sleep timing and amounts, other effects of SCID-diagnosed comorbid depression were observable the sleep data of these PTSD patients. REM density showed weak trends in the expected direction of elevation in the PTSD + MDD group, and SWS was approximately three times as abundant in the PTSD − MDD subjects. Preservation of SWS was particularly apparent in the PTSD patients denying a history of depression. PTSD + MDD and PTSD − MDD groups were also distinguished by mentalis EMG bursting during sleep, which was higher in the latter. Strong associations between dysphoria, as measured continuously by the BDI, and physiological markers measurable during sleep were also apparent. A strong positive correlation was observed between the BDI and baseline HR during both REM and stage 2 sleep. Though it achieved significance only for numbers of criterial epochs of oblique EOG activity per REM sleep epoch, the correlation between BDI and REM density was always positive. The last finding constitutes partial confirmation of Zarcone and Benson (1983), who also found positive correlations between computer-scored REM density and depression severity.

The findings of this study suggest first that the prominent heterogeneity of REM latency findings across studies of sleep in PTSD (reviewed in Ross et al 1989) is not due to sample differences in depressive comorbidity. Second, the absence of depression-related modification of REM sleep timing and abundance in these PTSD + MDD patients is reminiscent of the failure of PTSD patients with or without MDD to demonstrate hypercortisolemia and DST nonsuppression (Yehuda et al 1993a; Halbreich et al 1990). In contrast, our observations of REM density, SWS, and mentalis EMG suggest not all markers of depression are "overridden" in PTSD. The most straightforward interpretation of these results may be that a factor emerges in PTSD which exerts a specific effect upon REM sleep timing and amount, leaving intact other relationships between depression and sleep. It is tempting to speculate that this factor is related to the apparent increase in both tonic and phasic REM phenomena in the sleep of PTSD patients as compared to normal controls observed by Ross et al (1994). Understanding this factor may deepen our understanding of REM sleep architecture in both PTSD and other psychiatric disorders. In addition, it appears to be precisely those markers which some have claimed are associated with endogenous depression, REM latency reduction and DST nonsuppression (c.f. Giles et al 1987), that are not seen in PTSD + MDD patients. Clearly, it would be advantageous to have available DST findings in future studies of sleep and depression in PTSD.

In this study, SCID-diagnosed PTSD − MDD and PTSD + MDD groups did not exhibit statistically significant differences in baseline HR during sleep. When compared across conjointly diagnosed groups, HR differences were strengthened but still did not exceed nominal significance; nevertheless, large correlations between HR and BDI-indexed depression severity were observed. The large range in BDI scores in our sample (4–40) may have amplified such correlations; nevertheless, the finding of substantial positive correlation between BDI and HR would seem to contradict existing data suggesting the BDI taps "cognitive," as opposed to vegetative, features of depression (c.f. Louks et al 1989), at least in PTSD. An interesting possibility is that this correlation, between a vegetative marker and a "cognitive" factor in dysphoria, is specific to PTSD and perhaps is a clue to its pathophysiology. This relationship has not been reported in non-PTSD samples, and its existence would be surprising in light of the many opportunities there have been to observe it. The finding strengthens the suggestion extractable from the BDI data that there is an important component of dysphoria in PTSD patients that is not well captured by the MDD diagnosis. In this PTSD sample (excepting the never-depressed patients), this factor appears to be captured equally well by the BDI and MISS, judging from their high correlations and similar relations to both HR and mentalis EMG.

The HR observations also speak to an emerging debate in the literature on baseline HR in PTSD. Studies examining responses to trauma-related stimuli have consistently reported elevated resting HR in PTSD (c.f. Blanchard et al 1986). In contradiction to these findings, both McFall et al

(1992) and Orr (personal communication) have observed no differences in baseline HR between PTSD patients and controls when measurements were made under nonthreatening circumstances. Though there are no normative data on sleep HRs in this age group, studies of normals in their 20s have generally observed values of 57–59 BPM (Degaute et al 1991; Somers et al 1993). Though the mean sleep HR observed in this study of chronic severe PTSD inpatients was 65 BPM, the HRs of subjects with BDIs below 10 and MISS scores below 95 were approximately 58 BPM, agreeing well with those of young normals (see Figure 4a–b). Assuming there is no preferential relation between sleeping (as opposed to waking) HR and dysphoria, the findings of this study suggest that baseline HR in PTSD can only be evaluated with careful attention to mood status. It is also worth noting that very high BDI scores, such as some of those observed here, are sometimes accorded little validity in PTSD clinical settings, a prejudice called into question by these data.

EMG bursting during sleep was the biological variable demonstrating the greatest concordance across diagnostic and self-report measures of depression. Moreover, Figure 5c–d illustrates that three of five never-depressed subjects stood as far outliers in the bivariate distributions of mentalis EMG and dysphoria. Though further research will be required to confirm the degree of overlap between induced and spontaneous EMG, it is interesting to consider whether these outliers evidence an extension of the phenomenon noted by Schwartz et al (1978), Carney et al (1981), and Greden et al (1984) wherein elevated baseline facial EMG predicted better prognosis in depression. Conversely, the reduction of mentalis EMG bursting in association with more severe depression and/or more severe PTSD symptomology is reminiscent of data indicative of behavioral suppression in animal models of both depression and PTSD (c.f. Wiess et al 1980; Anisman and Catanzero 1978; Simson and Weiss 1988a). One might speculate that a connection exists between the attenuation of emotional experience observed in PTSD ("numbing") and attenuated spontaneous activity in the mimetic muscles during sleep. On a methodological note, the variability in EMG bursting under consideration here, on the order of +/−0.5 sec around a mean of 1 sec per 30-sec sleep epoch, is essentially invisible to visual sleep scoring.

Finally, certain observations point to the possibility that never-depressed PTSD patients are "special." These include their relative abundance of SWS, elevated mentalis EMG burst rates, and their overrepresentation among outliers in bivariate distributions of EMG versus BDI and MISS. In comparisons of SWS and mentalis EMG bursting, the never-depressed subjects seemed to account for PTSD − MDD/PTSD + MDD group differences, whereas remitted patients exhibited values close to those of currently depressed patients. This suggests SWS and EMG bursting may be *traits* in that they discriminate groups differing in lifetime, but not current, MDD. Like elevated facial EMG activity, elevated delta band EEG power has been associated with good prognosis in depression (Kupfer et al 1990). In view of these observations, chronic PTSD patients not meeting criteria for MDD, lifetime, may merit more focused investigations.

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